For receiving Office use only International Application No. REQUEST International Filing Date The undersigned requests that the present international application be processed Name of receiving Office and "PCT International Application" according to the Patent Cooperation Treaty. (if desired) (12 characters maximum) NEB-236-PCT TITLE OF INVENTION Box No. I MODULATION OF ENZYME ACTIVITY BY CHANGING RECIPROCAL STEREO-GEOMETRIC POSITIONS OF TWO CATALYTIC CENTERS IN AN ENZYME Box No. II APPLICANT This person is also inventor Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.) Telephone No. Facsimile No. NEW ENGLAND BIOLABS, INC. 32 Tozer Road Teleprinter No. Beverly, MA 01915 US Applicant's registration No. with the Office State (that is, country) of residence: State (that is, country) of nationality: US US the United States of America only the States indicated in the Supplemental Box all designated States except the United States of America This person is applicant for the purposes of: all designated States FURTHER APPLICANT(S) AND/OR (FURTHER) INVENTOR(S) Box No. III Name and address: (Family name followed by given name; for a legal entity, full official designation The address must include postal code and name of country. The country of the address indicated in this This person is: Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.) applicant only GUAN, Chudi applicant and inventor 10 Great Pond Road inventor only (If this check-box Wenham, MA 01984 is marked, do not fill in below.) US Applicant's registration No. with the Office State (that is, country) of residence: State (that is, country) of nationality: the States indicated in the Supplemental Box This person is applicant for the purposes of: all designated States except the United States of America the United States of America only all designated Further applicants and/or (further) inventors are indicated on a continuation sheet. AGENT OR COMMON REPRESENTATIVE; OR ADDRESS FOR CORRESPONDENCE Box No. IV The person identified below is hereby/has been appointed to act on behalf of the applicant(s) before the competent International Authorities as: common representative agent Telephone No. Name and address: (Family name followed by given name; for a legalentity, full official designation. The address must include postal code and name of country.) 978-927-5054 STRIMPEL, Harriet M. Facsimile No. New England Biolabs, Inc. 32 Tozer Road Teleprinter No. Beverly, MA 01915 US Agent's registration No. with the Office

Address for correspondence: Mark this check-box where no agent or common representative is/has been appointed and the space above is used instead to indicate a special address to which correspondence should be sent.

Addendum

1. Modulation of Enzyme Activity by Changing Reciprocal Stereo-Geometric Positions of Two Catalytic Centers in an Enzyme

Continuation of Box No. III FURTHER APPLICANT(S) AND/OR (FURTHER). INVENTOR(S)						
If none of the following sub-boxes is used, this sheet should	not be included in the request.					
Name and address: (Family name followed by given name; for a legal of the address must include postal code and name of country. The country of Box is the applicant's State (that is, country) of residence if no State of resid KUMAR, Sanjay 83 Old Right Road Ipswich, MA 01938 US	f the address indicated in this					
State (that is, country) of nationality:	State (that is, country) of residence:					
US	US					
This person is applicant all designated all design the Unite	the United States of America					
Name and address: (Family name followed by given name; for a legal The address must include postal code and name of country. The country Box is the applicant's State (that is, country) of residence if no State of res KUCERA, Rebecca 160 Woodland Mead Hamilton, MA 01982 US	of the address indicated in this					
State (that is, country) of nationality:	State (that is, country) of residence:					
US	mated States except Tax the United States the States indicated in					
This person is applicant for the purposes of: all designated all designated the Unit	the United States except ed States of America only the States indicated in the Supplemental Box					
Name and address: (Family name followed by given name; for a lega The address must include postal code and name of country. The country Box is the applicant's State (that is, country) of residence if no State of re	y of the address indicated in this					
State (that is, country) of nationality:	State (that is, country) of residence:					
This person is applicant for the purposes of: all designated all designated the United States all	ignated States except the United States the States indicated in the States of America only the Supplemental Box					
Name and address: (Family name followed by given name; for a leg The address must include postal code and name of country. The count Box is the applicant's State (that is, country) of residence if no State of r	ry of the address indicated in this					
State (that is, country) of nationality:	State (that is, country) of residence:					
This person is applicant all designated all designated the University of the purposes of:	signated States except inded States of America the United States of America only the States indicated in the Supplemental Box					
Further applicants and/or (further) inventors are indicated on another continuation sheet.						

Sheet No. ...3...

Box No. V DESIGNATIO	ONS				
The filing of this request constitutes under Rule 4.9(a), the designation of all Contracting States bound by the PCT on the international filing date, for the grant of every kind of protection available and, where applicable, for the grant of both regional and national patents.					
However,					
DE Germany is not design	gnated for any kind of nationa	al protection			
KR Republic of Korea is	not designated for any kind	of national protection			
RU Russian Federation is	s not designated for any kind	of national protection			
(The check-boxes above may be used to exclude (irrevocably) the designations concerned in order to avoid the ceasing of the effect, under the national law, of an earlier national application from which priority is claimed. See the Notes to Box No. V as to the consequences of such national law provisions in these and certain other States)					
Box No. VI PRIORITY	CLAIM				
The priority of the following ea	arlier application(s) is hereby	claimed:			
Filing date	Number		Vhere earlier application	is:	
of earlier application (day/month/year)	of earlier application	national application: country or Member of WTO	regional application:* regional Office	international application: receiving Office	
item (1) 21 November 2003 (21.11.2003)	60/524,123	US			
item (2)					
item (3)					
Further priority claims a	re indicated in the Supplemer	tal Box.	<u>.l</u>	1	
The receiving Office is requested to prepare and transmit to the International Bureau a certified copy of the earlier application(s) (only if the earlier application was filed with the Office which for the purposes of this international application is the receiving Office) identified above as: all items item(2) item(3) other, see Supplemental Box					
* Where the earlier application is an ARIPO application, indicate at least one country party to the Paris Convention for the Protection of Industrial Property or one Member of the World Trade Organization for which that earlier application was filed (Rule 4.10(b)(ii)):					
			<u> </u>		
Box No. VII INTERNATIONAL SEARCHING AUTHORITY					
Choice of International Searching Authority (ISA) (if two or more International Searching Authorities are competent to carry out the international search, indicate the Authority chosen; the two-letter code may be used):					
ISA /US					
Request to use results of ea International Searching Auto	arlier search; reference to the hority):				
Date (day/month/year)	Num	ber Cou	intry (or regional Office))	
Box No. VIII DECLARATIONS					
The following declarations are contained in Boxes Nos. VIII (i) to (v) (mark the applicable check-boxes below and indicate in the right column the number of each type of declaration): Number of declarations					
Box No. VIII (i)	Declaration as to the identi	ty of the inventor		:	
Box No. VIII (ii) Declaration as to the applicant's entitlement, as at the international filing date, to apply for and be granted a patent :					
Box No. VIII (iii) Declaration as to the applicant's entitlement, as at the international filing date, to claim the priority of the earlier application :					
Box No. VIII (iv) Declaration of inventorship (only for the purposes of the designation of the United States of America)				:	
Box No. VIII (v)	Declaration as to non-prej	udicial disclosures or exce	eptions to lack of novelty	y :	

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Sheet No.	4
SHOOTH IND	

Box No. IX CHECK LIST; LANGUAGE OF FILING						
This international application contains: (a) in paper form, the following number of sheets:	This international application is accompanied by the following item(s) (mark the applicable check-boxes below and indicate in right column the number of each item):	Number of items				
request (including	1. L fee calculation sheet	:				
declaration sheets) : 4	2. U original separate power of attorney	:				
description (excluding sequence listings and/or	3. X original general power of attorney	:				
tables related thereto) : 38	4. copy of general power of attorney; reference number, if any:					
claims : 6	5. statement explaining lack of signature					
abstract : 1	6. priority document(s) identified in Box No. VI as					
drawings : 22	item(s):					
Sub-total number of sheets: 71	7. translation of international application into					
sequence listings : tables related thereto :	(language):					
(for both, actual number of	8. separate indications concerning deposited microorganism or other biological material	· :				
sheets if filed in paper form, whether or not also filed in	9. Sequence listings in computer readable form (indicate type and number of carriers)					
computer readable form; see (c) below)	(i) X copy submitted for the purposes of international search	h under				
Total number of sheets : 71	Rule 13ter only (and not as part of the international a	pplication): 12				
(b) only in computer readable form	(ii) (only where check-box (b)(i) or (c)(i) is marked in lef additional copies including, where applicable, the cop purposes of international search under Rule 13ter	py for the :				
(Section 801(a)(i)) (i) sequence listings	(iii) X together with relevant statement as to the identity of copies with the sequence listings mentioned in left co	the copy or lumn : 2				
(ii) tables related thereto (c) also in computer readable form	10. tables in computer readable form related to sequence list (indicate type and number of carriers)					
(Section 801(a)(ii)) (i) sequence listings	(i) copy submitted for the purposes of international sear Section 802(b-quater) only (and not as part of the int	ch under ernational				
(ii) tables related thereto	application)	:				
Type and number of carriers (diskette, CD-ROM, CD-R or other) on which are contained the	(ii) (only where check-box (b)(ii) or (c)(ii) is marked in left column) additional copies including, where applicable, the copy for the purposes of international search under Section 802(b-quater)					
sequence listings:	(iii) together with relevant statement as to the identity of the copy or					
tables related thereto: copies with the tables mentioned in left column						
(additional copies to be indicated under items 9(ii) and/or 10(ii), in right column)	(additional copies to be indicated under items 9(ii) and/or 10(ii), in right column) 11. \(\text{\tex{\tex					
Figure of the drawings which	Language of filing of the					
should accompany the abstract: 12	international application: English					
Box No. X SIGNATURE OF APPLICA	NT, AGENT OR COMMON REPRESENTATIVE gning and the capacity is not obvious fro	m reading the request).				
Next to each signature, matche me name of the person si						
	#Zmes O muzex					
	Harriet M. Strimpel, Chief Patent C	counsel and				
	Assistant Clerk					
	For receiving Office use only					
1 Deta of actual action of the country of	For receiving Office use only	2. Drawings:				
Date of actual receipt of the purported international application:	Z. Diawnigs.					
rea						
Corrected date of actual receipt due to later but timely received papers or drawings completing the purported international application:						
4. Date of timely receipt of the required corrections under PCT Article 11(2):						
5. International Searching Authority (if two or more are competent): ISA / 6. Transmittal of search copy delayed until search fee is paid						
	For International Bureau use only					
Date of receipt of the record copy by the International Bureau:						

This sheet is not part of and does not count as a sheet of the international application.

PCT For receiving Office use only FEE CALCULATION SHEET International Application No. Annex to the Request Applicant's or agent's NEB-236-PCT file reference Date stamp of the receiving Office Applicant NEW ENGLAND BIOLABS, INC., et al. CALCULATION OF PRESCRIBED FEES 300.00 T 1. TRANSMITTAL FEE..... 1.000.00 S 2. SEARCH FEE.... International search to be carried out by (If two or more International Searching Authorities are competent to carry out the international search, indicate the name of the Authority which is chosen to carry out the international search.) 3. INTERNATIONAL FILING FEE Where item (b) and/or (c) of Box No. IX apply, enter Sub-total number of sheets Where item (b) and (c) of Box No. IX do not apply, enter Total number of sheets 1,134.00 ii 492.00 number of sheets additional component (only if sequence listings and/or tables related thereto are filed in computer readable form under Section 801(a)(i), or both in that form and on paper, under Section 801(a)(ii)): i3 1,626.00 1 Add amounts entered at i1, i2 and i3 and enter total at I (Applicants from certain States are entitled to a reduction of 75% of the international filing fee. Where the applicant is (or all applicants are) so entitled, the total to be entered at I is 25% of the international filing fee.) 20.00 P 4. FEE FOR PRIORITY DOCUMENT (if applicable) **USD** 2,946.00 Add amounts entered at T, S, I and P, and enter total in the TOTAL box MODE OF PAYMENT authorization to charge deposit account (see below) postal money order cash coupons X cheque bank draft revenue stamps other (specify): AUTHORIZATION TO CHARGE (OR CREDIT) DEPOSIT ACCOUNT Receiving Office: RO/ _ (This mode of payment may not be available at all receiving Offices) Deposit Account No.: 14-0740 Authorization to charge the total fees indicated above. Date: 22 November 2004 (This check-box may be marked only if the conditions for deposit accounts of the receiving Office so permit) Authorization to charge any deficiency Name: Harriet M. Strimpel or credit any overpayment in the total fees indicated above. Authorization to charge the fee for priority document. Signature: